

91. (New) A method according claim 84, wherein the biological composition comprises a blood product.

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93. (New) A method according to claim 91, wherein the blood composition flows through the system as a result of a pressure differential which arises due to a hydrostatic head.

94. (New) A method according to claim 91, wherein the blood composition flows through the system as a result of a pressure differential which arises due to the use of a pump.

95. (New) A method according to claim 91, wherein the blood composition flows through the system at a flux between about 0.1 mL/cm<sup>2</sup>/min and about 10 mL/cm<sup>2</sup>/min.

96. (New) A method according to claim 95, wherein the blood composition flows through the system at a flux between about 0.2 mL/cm<sup>2</sup>/min and about 5 mL/cm<sup>2</sup>/min.

97. (New) A method according to claim 91, wherein the blood composition contains an original amount of factor XI and said blood composition has at least about 91% of said original amount of factor XI after said treating with said system.

#### REMARKS

Applicants have filed a copy of the original application along with a publication copy denoted "Publication Copy" which includes new claims and formal drawings. No new matter is believed to be entered. This application has been filed to allow the consideration of references not cited previously.

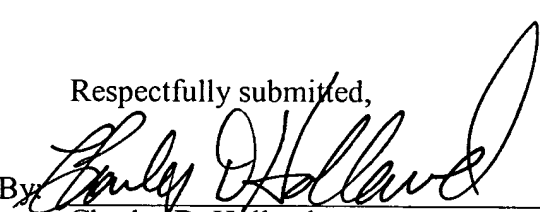
In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned attorney so that prosecution may be expedited. Attached to this Amendment is a sheet entitled "Attachment Of Amendments Showing Changes."

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 282172000404. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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Attachment Of Amendments Showing Changes

10016323-121001

## ATTACHMENT OF AMENDMENTS SHOWING CHANGES

In the Title:

--ADSORBING PATHOGEN-INACTIVATING COMPOUNDS WITH POROUS PARTICLES IMMOBILIZED IN A MATRIX--

In the Specification:

Please replace the first paragraph as follows:

--This application is a continuation application of copending application Serial No. 09/112,068 filed July 8, 1998, which is a continuation-in-part application of copending application Serial Number 09/003,113, filed January 6, 1998 now abandoned, each of which is incorporated by reference in its entirety.--

In the Abstract:

--Methods and devices are provided for reducing the concentration of low molecular weight compounds in a biological composition, while substantially maintaining a desired biological activity of the biological composition. The device comprises highly porous adsorbent particles, and the adsorbent particles are immobilized by an inert matrix. The matrix containing the particles is contained in a housing, and the particles range in diameter from about 1  $\mu\text{m}$  to about 200  $\mu\text{m}$ . the matrix can be fibrous, and the particles can have a surface area greater than 750  $\text{m}^2/\text{g}$  and a pore diameter between about 25 and 800  $\text{\AA}$ . the device can be used to adsorb and remove a pathogen-inactivating compound that is a nucleic acid-binding compound such as psoralen, and acridine derivative or a dye from a biological composition such as a blood product.--

In the Claims:

58. (New) A pathogen-inactivating compound adsorption system for reducing the concentration of a low molecular weight pathogen-inactivating compound in a biological composition, wherein the pathogen-inactivating compound adsorption system comprises a housing compatible with the biological composition and containing an adsorption medium

comprising adsorbent resin particles having a network pore structure immobilized by a matrix, wherein the diameter of the adsorbent particles ranges from about 1  $\mu$ m to about 200  $\mu$ m, wherein the adsorbent particles have an affinity for said pathogen-inactivating compound, wherein the system is configured to remove said pathogen-inactivating compound from said biological composition in a flow process, and wherein the system is configured so that the biological composition treated with the system maintains sufficient biological activity so that said biological composition is suitable for infusion within a human.

59. (New) A system according to claim 58, wherein the matrix comprises a sintered polymeric matrix.

60. (New) A system according to claim 59, wherein the diameter of the adsorbent particles is between about 50 and 150  $\mu$ m.

61. (New) A system according to claim 58, wherein the matrix comprises a fibrous matrix.

62. (New) A system according to claim 61, wherein the diameter of the adsorbent particles is between about 1 and 50  $\mu$ m and the matrix comprises cellulose fibers.

63. (New) A system according to claim 61, wherein the particle containing matrix is composed of a plurality of layers.

64. (New) A system according to claim 61, wherein the fibrous matrix comprises a synthetic polymer fiber having a polymer core with a high melting temperature surrounded by a sheath with a lower melting temperature.

65. (New) A system according to claim 59 or claim 61, wherein the particle containing matrix is at least 3 mm thick.

66. (New) A system according to claim 59 or 61, wherein the adsorbent resin particles have a surface area greater than about 750 m<sup>2</sup>/g, and the porous adsorbent particles are between 30 and 70 percent of the weight of the adsorption medium.

67. (New) A system according to claim 59 or 61, wherein the matrix contains said adsorbent particles.

68. (New) A system according to claim 67, wherein the adsorbent resin particles have a surface area greater than about 750 m<sup>2</sup>/g.

69. (New) A system according to claim 68, wherein the adsorbent resin particles are polyaromatic.

70. (New) A system according to claim 69, wherein said adsorbent resin particles have a pore diameter between about 25 and 800 Å.

71. (New) A system according to claim 70, wherein said adsorbent resin particles have a pore diameter between about 25 and 150 Å.

72. (New) A system according to claim 71, wherein said adsorbent resin particles have a pore diameter between about 25 and 50 Å.

73. (New) A system according to claim 68, wherein the adsorbent resin particles do not require prewetting before use.

74. (New) A system according to claim 68, wherein the adsorbent resin particles are hypercrosslinked.

75. (New) A system according to claim 58, 59, or 61 wherein the pathogen inactivating compound comprises a nucleic acid-binding compound.

76. (New) A system according to claim 75, wherein the nucleic acid-binding compound comprises a psoralen.

77. (New) A system according to claim 75, wherein the nucleic acid-binding compound comprises an acridine derivative.

78. (New) A system according to claim 75, wherein the nucleic acid-binding compound comprises a dye.

79. (New) A system according to claim 75, wherein the adsorbent resin particles have an affinity for a nucleic acid-binding compound having an electrophilic group capable of reacting with a nucleophilic group of a quencher that quenches undesired side reactions of the pathogen-inactivating compound.

80. (New) A system according to claim 79, wherein the adsorbent resin particles additionally have an affinity for said quencher.

81. (New) A system according to claim 75, wherein the adsorbent resin particles additionally have an affinity for a degradation product of said nucleic acid-binding compound.

82. (New) A method for reducing the concentration of a low molecular weight compound comprising a pathogen-inactivating compound in a biological composition, said method comprising treating the biological composition with a system of claim 58, 59, or 61, wherein the biological composition treated with the system maintains sufficient biological activity so that said biological composition is suitable for infusion within a human.

83. (New) A method for reducing the concentration of a low molecular weight compound comprising a nucleic acid-binding compound in a biological composition, said method comprising treating the biological composition with a system of claim 75, wherein the biological composition treated with the system maintains sufficient biological activity so that said biological composition is suitable for infusion within a human.

84. (New) A method for reducing the concentration of a low molecular weight compound comprising a psoralen nucleic acid-binding compound in a biological composition, said method comprising treating the biological composition with a system of claim 75, wherein the biological composition treated with the system maintains sufficient biological activity so that said biological composition is suitable for infusion within a human.

85. (New) A method according to claim 84, wherein no more than about ten percent of an amount of said psoralen nucleic acid-binding compound originally added to said biological composition remains as free psoralen in said biological composition.

86. (New) A method according to claim 84, wherein said psoralen nucleic acid-binding compound is selected from the group consisting of 4'-(4-amino-2-oxa)butyl-4,5',8-trimethyl psoralen, 8-methoxypsoralen, halogenated psoralens, isopsoralens and psoralens linked to quaternary amines, 5'-bromomethyl-4,4',8-trimethylpsoralen, 4'-bromomethyl-4,5',8-trimethylpsoralen, 4'-(4-amino-2-aza)butyl-4,5',8-trimethylpsoralen, 4'-(2-aminoethyl)-4,5',8-

trimethylpsoralen, 4'-(5-amino-2-oxa)pentyl-4,5',8-trimethylpsoralen, 4'-(5-amino-2-aza)pentyl-4,5',8-trimethylpsoralen, 4'-(6-amino-2-aza)hexyl-4,5',8-trimethylpsoralen, 4'-(7-amino-2,5-oxa)heptyl-4,5',8-trimethylpsoralen, 4'-(12-amino-8-aza-2,5-dioxa)dodecyl-4,5',8-trimethylpsoralen, 4'-(13-amino-2-aza-6,11-dioxa)tridecyl-4,5',8-trimethylpsoralen, 4'-(7-amino-2-aza)heptyl-4,5',8-trimethylpsoralen, 4'-(7-amino-2-aza-5-oxa)heptyl-4,5',8-trimethylpsoralen, 4'-(9-amino-2,6-diazav)nonyl-4,5',8-trimethylpsoralen, 4'-(8-amino-5-aza-2-oxa)octyl-4,5',8-trimethylpsoralen, 4'-(9-amino-5-aza-2-oxa)nonyl-4,5',8-trimethylpsoralen, 4'-(14-amino-2,6,11-triaza)tetradecyl-4,5',8-trimethylpsoralen, 5'-(4-amino-2-aza)butyl-4,4',8-trimethylpsoralen, 5'-(6-amino-2-aza)hexyl-4,4',8-trimethylpsoralen and 5'-(4-amino-2-oxa)butyl-4,4',8-trimethylpsoralen.

87. (New) A method according to claim 83 wherein the low molecular weight compound comprises an acridine derivative.

88. (New) A method according to claim 87, wherein the acridine derivative comprises N-(9-acridinyl)- $\beta$ -alanine.

89. (New) A method according to claim 83, wherein the low molecular weight compound comprises a dye.

90. (New) A method according to claim 89, wherein the dye comprises methylene blue.

91. (New) A method according claim 84, wherein the biological composition comprises a blood product.

92. (New) A method according to claim 91, wherein the blood product consists essentially of plasma.

93. (New) A method according to claim 91, wherein the blood composition flows through the system as a result of a pressure differential which arises due to a hydrostatic head.

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95. (New) A method according to claim 91, wherein the blood composition flows through the system at a flux between about 0.1 mL/cm<sup>2</sup>/min and about 10 mL/cm<sup>2</sup>/min.

96. (New) A method according to claim 95, wherein the blood composition flows through the system at a flux between about 0.2 mL/cm<sup>2</sup>/min and about 5 mL/cm<sup>2</sup>/min.

97. (New) A method according to claim 91, wherein the blood composition contains an original amount of factor XI, and said blood composition has at least about 91% of said original amount of factor XI after said treating with said system.

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